TRANSMITTAL OF APPEAL BRIEF (Large Entity)

Docket No. CARD-1002US

In Re Application Of:

Ronald S. Vladyka, Jr., et al.

Serial No.	Filing Date	Examiner	Group Art Unit
09/708,581	November 9, 2000	Everett White	1623

Invention:

MICROCRYSTALLINE CELLULOSE CUSHIONING GRANULES

TO THE COMMISSIONER FOR PATENTS:

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DOCKET NO.: CARD-1002US PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: **Ronald S. VLADYKA, Jr., et al.**

Serial No.: **09/708,581** Group Art Unit: **1623**

Filed: **November 9, 2000** Examiner: **Everett White**

Entitled: **MICROCRYSTALLINE CELLULOSE CUSHIONING GRANULES**

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APPEAL BRIEF UNDER 37 C.F.R. § 1.191

This is an appeal from the rejections set forth in the Final Rejection dated January 15, 2004 (hereinafter "the Final Rejection"). This Appeal Brief is being filed within two months of the filing of a Notice of Appeal on April 15, 2004, and thus is timely. Appellant respectfully submits that the rejections in the Final Rejection were made in error, and that these rejections should be reversed for the reasons set forth below.

I. The Real Party in Interest

The real party in interest in the present appeal is R.P. Scherer Technologies, Inc., 2030 East Flamingo Road, Suite 260, Paradise Valley, Nevada 89119, to whom an undivided interest in the above-captioned application has been assigned by virtue of an assignment by the inventors to the FMC Corporation recorded on January 23, 2001, at reel 011469, frame 0055, and a subsequent assignment from the FMC Corporation to R.P. Scherer Technologies, Inc, recorded on May 7, 2002, at reel 012884, frame 0216.

II. Related Appeals and Interferences

The Appellant is unaware of any pending appeals or interferences related to the present appeal.

III. The Status of the Claims

Claims 1 through 26 are currently pending in the present application and stand rejected in a Final Rejection dated January 15, 2004. The rejection of claims 1 through 26 is hereby appealed. A copy of the currently pending claims 1 through 26 is attached as an appendix hereto.

IV. The Status of any Amendments Filed after Final Rejection

No amendments were filed after the Final Rejection of 01/15/2004.

V. Summary of the Invention

The microcrystalline cellulose granules of the present invention may be employed as a component in a tablet, for example, designed for the controlled release of a vitamin or pharmaceutical composition. See page 1, lines 6-9 of the specification. The microcrystalline cellulose granules of the invention may be used in such tablets as cushioning granules, for the purpose of protecting the controlled release particles of the tablet during the application of pressure in the process of forming of the tablet. See page 1, lines 6-9 of the specification. It has been found that microcrystalline cellulose granules made in accordance with the process of the present invention and having the properties of the product of claims 16-24 of the present application, help to protect controlled release particles from damage or destruction during the application of pressure, for example, in a tabletting process, thereby substantially maintaining the controlled release properties of such controlled release particles when the particles are incorporated in a tablet. See e.g. the Examples on pages 11-18 of the specification. This permits the formulation of certain controlled release vitamins and pharmaceuticals in tablet form using existing tableting operations, which tablet provides the desired controlled release of the actives. See page 2, lines 23-27 of the specification. This is in contrast to the administration of these products in a hard gelatin capsule containing a plurality of the controlled release particles. See the specification at page 2, lines 5-15 for example.

The claimed drying steps of the process of the present invention are important because they provide improved cushioning properties to the microcrystalline cellulose. See e.g. the examples on pages 11-18 of the specification. This is believed to be the result of less water from

the granulating fluid being hydrogen bonded to the microcrystalline cellulose cushioning material, as compared to the use of a drying process, which does not remove the organic component of the granulating fluid at a controlled rate with no heat input. See e.g. specification at page 6, lines 14-19. Hydrogen bonding between the water component and the microcrystalline cellulose generally leads to denser, less porous granules which may not provide as much cushioning when employed in a tablet, as compared to granules dried using the drying process of the present invention. See page 6, lines 14-19 of the specification.

In a second aspect, as claimed in independent claim 16, the present invention relates to porous, microcrystalline cellulose granules having an irregular shape. The granules have a loose bulk density of from about 0.2 g/cc to about 0.4 g/cc and a mean particle size of from about 250 microns to about 1500 microns. The granules are of irregular shape and wide particle size distribution which promotes packing and cushioning in tablets made with the claimed microcrystalline cellulose. See page 4, lines 14-18 and page 7, lines 19-24 of the specification. Additional features of this aspect of the invention are claimed in claims 17 through 24.

VI. Issues on Appeal

Appellant believes that the various issues to be considered on appeal may be concisely summarized as follows:

Issue 1: Whether claims 1, 2 and 4-11 are unpatentable under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,123,964, issued to Asgharnejad et al. (hereinafter "Asgharnejad et al.").

Issue 2: Whether claims 1 to 13 are unpatentable under 35 U.S.C. § 103(a), as obvious over Asgharnejad et al...

Issue 3: Whether claim 3 is unpatentable unpatentable under 35 U.S.C. § 103(a) as obvious over Asgharnejad et al. in view of U.S. Patent No: 6,384,020 issued to Flanner et al. (hereinafter "Flanner et al.").

Issue 4: Whether claims 12 and 13 are unpatentable under 35 U.S.C § 103(a) as obvious over Asgharnejad et al. in view of U.S. Patent No. 5,725,886, issued to Erkoboni et al. (hereinafter "Erkoboni et al.").

Issue 5: Whether claims 14-16, and 18-26 are unpatentable under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 6,149,943, issued to McTeigue et al. (hereinafter "McTeigue et al.").

Issue 6: Whether claim 17 is unpatentable under 35 U.S.C. § 103(a) as obvious over McTeigue et al. in view of U.S. Patent No. 6,117,451, issued to Kumar (hereinafter "Kumar").

VII. Grouping of Claims

Group I – Claims 1-2, 4-8, and 10-13.

Group II – Claim 3.

Group III – Claim 9.

Group IV – Claims 14-16, 18 and 20-26

Group V – Claim 19

Group VI – Claim 17

VIII. Argument

Issue 1: Whether claims 1, 2 and 4-11 are unpatentable under 35 U.S.C. § 102(e) as being anticipated by Asgharnejad et al.

A. The Rejection

Claims 1, 2, and 4-11 have been rejected under 35 U.S.C. § 102(e) as being unpatentable over Asgharnejad et al. The rationale for this rejection was originally set forth in the Office Action dated July 15, 2003, as follows:

> "The Asgharnejad et al patent discloses a process comprising the steps of (1) forming a powder blend of the active ingredient with a binder/diluent, a first diluent, a second diluent and a disintegrant, using a mixer; (2) wet granulating the powder blend by adding a solution of ethanol/water to the powder blend; (3) drying the granules to remove the ethanol/water with heated air in a fluid bed dryer or tray dryer (see column 2, line 63 to column 3, line 6). See column 3, lines 21-29 of the Asgharnejad et al patent wherein the binder/diluent is pregelatinized starch; the first diluent is microcrystalline cellulose; and wherein it is indicated that the solution of ethanol/water is in a range of 0% to 80% ethanol in water (w/w). The ethanol/water solution used in the Asgharnejad et al patent meets the polar organic solvent requirement disclosed in the claims..."

See page 4, lines 5-15 of the July 15, 2003 Office Action

In response to this rejection of July 15, 2003, Applicant amended claim 1 to include the limitation that the drying step (b) be conducted "with no heat input at ambient temperature." The Examiner, in the Final Rejection, maintained the rejection. The rationale for maintaining the rejection was set forth in the Final Rejection, as follows:

> "Applicant's [sic] arguments filed October 15, 2003 have been fully considered but they are not persuasive. Applicants amended the claimed invention by adding the language "with no heat input at ambient temperature" and argues that the Asgharnejad et al patent uses heated air for its drying step which is different from

amended claim 1 which provides for "no heat input at ambient temperature". This argument is not persuasive since it is unclear how ambient temperature was reached or how the ambient temperature is maintained without some sort of temperature control. Is the drying step carried out at room temperature? If so is the room temperature the same as the temperature outside the immediate location of the drying step? It is noted that the drying step in Example 1 of the instant specification is carried out for 16 hours. What type of system is Applicants [sic] using to maintain ambient temperature for this length of time? Does the ambient temperature used in the drying step comprise a wide range of temperature values?

Applicants argue that Asgharnejad is only concerned with removing the ethanol/water granulating fluid and contains no teaching that it is important or desirable to remove the ethanol component of the granulating fluid at a controlled rate. This argument is not persuasive since Asgharnejad teaches carrying out a drying step that can take up to 24 hours, which suggests drying at a controlled rate.

Applicants argue that Asgharnejad exemplifies only a single step. This argument is not persuasive since the minimal amount of water used as a granulating fluid with the polar solvent set forth in the instant claims is 15 parts water as described in the water to polar organic solvent ratio of 15:85. The percent composition with the ethanol and water as an azeotropic liquid in the CRC Handbook shows that the instant claims set forth an excessive amount of water. By having an excess amount of water, steps (b) and (c) of the instant claims only set forth a normal drying procedure for removing azeotropic liquids containing ethanol and water wherein there is an excess amount of water. Once all the azeotropic liquid (ethanol/water combination) is removed, the excess amount of water in the process still remains in the drying vessel, which applicants removes [sic] in step (c). The Asgharnejad et al patent also contains an excess of water along with the ethanol and water azeotrope combination. See column 3, line 28 of the Asgharnejad et al patent wherein the combination of ethanol and water may preferably comprise as low as 5% ethanol, which is well within the range of having excess water with an azeotrope of ethanol and water. The excess water set forth in the granulating fluid of the instant claims causes the extra process step (step c) in the instant claims which would be an inherent feature of the process set forth in the Asgharnejad et al patent since the Asgharnejad et al patent also discloses excess water in the granulating fluid.

See page 3, lines 5-25 of the Final Rejection.

B. Groups 1-2 – Claims 1-2 and 4-13

Claim 1 is novel over Asgharnejad et al. simply because there is no teaching or suggestion in Asgharnejad et al. to dry granulated microcrystalline cellulose at a controlled rate with no heat input. Asgharnejad et al. teaches drying wet granules at about 47°C for 3.0 hours. See column 39, lines 28-30 of Asgharnejad et al. Column 3, lines 5-6 of Asgharnejad et al. indicate that the drying time may be from 10 minutes to 24 hours with heated air in a fluid bed dryer or tray dryer. Nowhere in Asgharnejad et al. does there appear any teaching of drying granulated mircocrystalline cellulose at a controlled rate with no heat input for a time sufficient to remove at least substantially all of the polar organic solvent without removing a substantial portion of the water as the instant invent requires. Even assuming *arguendo*, that the Examiner's characterization for the Asgharnejad et al. process is correct, that the polar organic solvent and the water are removed in a two step process, the instant claims require "no heat input," and this element of the claims is simply not found in Asgharnejad et al.

The Examiner raised several questions about ambient temperature and room temperature in the Final Rejection. It is not important how ambient temperature is achieved in the context of the present invention, but rather only that a claimed drying step be carried out with no heat input at ambient temperature. Ambient temperature is a well-known term that can be found in any dictionary. If the Examiner is attempting to assert that the 47°C temperature used in the drying process of Asgharnejad et al. is "ambient temperature," there is no support for this conclusion in the record. 47°C is a very high temperature which would not be considered to be "ambient temperature" i.e. the temperature of the surroundings, by a person of ordinary skill in the art. The

Examiner has offered no evidence to the contrary and thus, if this is the Examiner's position, it should be disregarded as totally unsupported by evidence.

It should also be noted that it appears that the Examiner has admitted that claims 1-13 are novel over Asgharnejad et al. at page 6, lines 7-17 of the July 15, 2003 Office Action, as quoted below in relation to Issue 2.

Claims 2 and 4-13 all depend from claim 1 and thus are considered novel over Asgharnejad et al. for at least the same reason as given for claim 1 above. Favorable consideration and reversal of the rejection of claims 1-2 and 4-13 under 35 U.S.C. §102(e) over Asgharnejad et al. is requested.

Issue 2: Whether Claims 1 to 13 are obvious over Asgharnejad et al.

A. The Rejection

Claims 1-13 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Asgharnejad et al. The rationale for this rejection was set forth in the Office Action dated July 15, 2003, as follows:

> "The Asgharnejad et al patent discloses a process comprising the steps of (1) forming a powder blend of the active ingredient with a binder/diluent, a first diluent, a second diluent and a disintegrant, using a mixer; (2) wet granulating the powder blend by adding a solution of ethanol/water to the powder blend; (3) drying the granules to remove the ethanol/water with heated air in a fluid bed dryer or tray dryer (see column 2, line 63 to column 3, line 6). See column 3, lines 21-29 of the Asgharnejad et al patent wherein the binder/diluent is pregelatinized starch; the first diluent is microcrystalline cellulose; and wherein it is indicated that the solution of ethanol/water is in a range of 0% to 80% ethanol in water (w/w). The ethanol/water solution used in the Asgharnejad et al patent meets the polar organic solvent requirement disclosed in the claims..."

See page 6, lines 7-17 of the July 15, 2003, Office Action.

The Examiner goes on to state:

> The method of the instant claims differ from the process of Asgharnejad et al patent since Asgharnejad et al further discloses the presence of an active ingredient as part of the process medium and includes the steps that lead to the preparation of a tablet which is not set forth in the instantly claimed method. However, the active ingredient and additional process medium does not negate the preparation of microcrystalline cellulose granules in the Asgharnejad et al patent. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant(s) [sic] invention having the Asgharnedjad [sic] et al patent before him to replace the ethanol and water solution having an active ingredient of the Asgharnedjad [sic] patent with only ethanol and water in view of their closely related structures and the resulting expectation of similar granulating properties. One having ordinary skill in the art would have been motivated to employ the process of the prior art with the expectation of obtaining the desired product because the skilled artisan would have expected the analogous starting materials to react similarly.

See page 7, lines 11-25 of the July 15, 2003 Office Action.

B. Group I – Claims 1-2, 4-8 and 10-13

The Examiner's rejection is not understood, because it seems that the Examiner takes the position that all a skilled person has to do to arrive at the present invention is to remove the active ingredient of the composition of Asgharnejad et al. as the Examiner stated in his rejection:

> "However, the active ingredient and additional process medium does not negate the preparation of microcrystalline cellulose granules in the Asgharnejad et al patent. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant(s) [sic] invention having the Asgharnedjad [sic] et al patent before him to replace the ethanol and water solution having an active ingredient of the Asgharnedjad [sic] patent with only ethanol and water in view of their closely related structures and the resulting expectation of similar granulating properties. One having ordinary skill in the art would have been motivated to employ the process of the prior art with the expectation of obtaining the desired product

> because the skilled artisan would have expected the analogous starting materials to react similarly."

See page 7, lines 11-25 of the July 15, 2003 Office Action

Thus it appears that the Examiner is arguing that it would be obvious to remove the active ingredient of the Asgharnejad et al. composition to arrive at the present invention. This argument is flawed for several reasons.

First, since Asgharnejad et al. is directed to the preparation of granulated compositions that include growth hormones, a skilled person would not remove the active ingredient, i.e. growth hormone, from the composition of Asgharnejad et al. for the simple reason that this would defeat the entire purpose of Asgharnejad et al.

Second, the Examiner has not made out a *prima facie* case of obviousness for at least the following reasons. It is well-established that:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.
> The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure.

In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991), *quoted in* M.P.E.P. § 2143.

It is similarly well-established that, "if the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence" of non-obviousness. *See* M.P.E.P. § 2142.

Asgharnejad et al. does not teach or suggest conducting the drying of the granulated microcrystalline cellulose to at a controlled rate with no heat input. The general teaching of Asgharnejad et al. requires drying in heated air and the exemplified drying process of Asgharnejad et al. is carried out at 47°C for 3 hours. The use of heated air to provide a drying environment of 47°C, i.e. significantly above ambient temperature, for a period of 3 hours, as in Asgharnejad et al., involves heat input and thus does not meet the limitation of claims 1-2, 4-8 and 10-13 requiring " drying at a controlled rate with no heat input."

Thus, not only does Asgharnejad et al. teach a skilled person to use heat in the drying process, Asgharnejad et al. nowhere suggests to the skilled person to dry with no input of heat. Under these circumstances, it is clear that Asgharnejad et al. teaches away from the present invention and that a skilled person, following the teachings of Asgharnejad et al. would use heat input in the drying process, contrary to the requirement of claims 1-2, 4-8 and 10-13 of the present application.

The Examiner also took the position that,

> Applicants argue that Asgharnejad exemplifies a single step. This argument is not persuasive since the minimal amount of water used as a granulating fluid with the polar solvent set forth in the instant claims is 15 parts water as described in the water to polar organic solvent ratio of 15:85. The percent composition with the ethanol and water as an azeotropic liquid in the CRC Handbook shows that the instant claims set forth an excessive amount of water. By having an excess amount of water, steps (b) and (c) of the instant claims only set forth a normal drying procedure for removing azeotropic liquids containing ethanol and water wherein there is an excess amount of water. Once all the azeotropic liquid (ethanol/water combination) is removed, the excess amount of water in the process still remains in the drying vessel, which applicants [sic] removes in step (c). The Asgharnejad et al patent also contains an excess of water along with the ethanol and water azeotrope combination. See column 3, line 28 of the Asgharnejad patent wherein

> the combination of ethanol and water may preferable comprise as low as 5% ethanol, which is well within the range of having excess water with an azeotrope of ethanol and water. The excess water set forth in the granulating fluid of the instant claims cause the extra process step (step c) in the instant claims which would be an inherent feature of the process set forth in the Asgharnejad et al patent since the Asgharnejad et al patent also discloses excess water in the granulating fluid.

See the Final Rejection at page 3, lines 6-26. This reasoning, however, ignores the fact that Asgharnejad et al. does not teaching drying with no heat input, as required by the claims. Moreover, it is pure speculation on the part of the Examiner that the granulating fluid contained in the granulate will behave as a solvent mixture during the drying step. The Examiner has not offered any evidence in support of this underlying assumption. In fact, whether the granulating fluid behaves as a solvent mixture during the granulating step, may depend on a number of factors such as the amount of granulating fluid used in the granulating step relative to the amount of solid material in the granulated mixture, whether and how much ethanol and/or water is adsorbed on the microcrystalline cellulose, the degree of hydrogen bonding between the ethanol and the microcrystalline cellulose, the degree of hydrogen bonding between the water and the microcrystalline cellulose, as well as the conditions to which the granulated mixture is subjected.

The skilled person will expect from a common general knowledge of chemistry that polar molecules, such as ethanol and water, would tend to hydrogen bond with and/or adsorb onto the surface of cellulosic materials, in which case the hydrogen bonded ethanol/water granulating fluid will not behave as a solvent mixture during the drying step. Thus, the Examiner's underlying assumption that the ethanol/water granulating fluid

of Asgharnejad et al. will behave as a solvent mixture during the Asgharnejad et al. drying step is highly questionable since it is completely unsupported by evidence and because statements made in the specification, as well as the common general knowledge of a skilled person, tend to contradict the assumption. Therefore, the Examiner's position that the drying step of Asgharnejad et al. is the same as that of claim 1 should be disregarded for this additional reason.

In addition, the present specification contains examples that demonstrate the benefits of the claimed process, relative to a process which dries the microcrystalline cellulose granules with heat input in a single step, similar to the process of Asgharnejad et al. Comparative Examples B-C employed a one-step drying process very similar to the process of Asgharnejad et al., i.e. the granulates were tray dried overnight at 50°C. This drying temperature is very close to the 47°C drying temperature of the drying step employed in the examples of Asgharnejad et al. Moreover, drying overnight, (i.e. up to 16 hours) falls clearly within the 10 minutes to 24 hour drying period disclosed by Asgharnejad et al. at col. 3, lines 4-6.

Upon tabletting of the compositions dried by the methods of Comparative Examples B-C, it was found that, "Both sets of tablets [sic – granules] were found to be too dense to provide adequate cushioning properties."[1] Thus, Comparative Examples B-C

[1] Comparative Examples B-C erroneously refer to the "tablets" as being too dense to provide adequate cushioning properties. From a reading of the specification, it is clear that it is the granules that provide cushioning properties when incorporated in tablets. See e.g. page 6, lines 15-19 of the specification. Thus, the skilled person would understand that Comparative Examples B-C teach that the granules, not the tablets, were too dense to provide adequate cushioning properties. On April 25, 2003, the Appellant filed an Amendment After Final Rejection for the purpose of correcting this minor typographical error in Comparative Examples B-C.

confirm the conclusion at page 6, lines 15-19 of the specification that use of a single step drying process without a controlled rate drying step such as is disclosed by Asgharnejad et al. produces a dense microcrystalline cellulose granule that exhibits poor cushioning properties for protecting controlled-release particles from destruction due to the application of pressure during a tabletting process.

Table 1 summarizes the quantities of the material used in each granulation and the properties of the MCC granules produced. There are no differences in the quantities of the materials. The differences between the tablets in Examples B and C as well as examples 3, 4, 5 and 7 are in the compression force applied during tabletting, and that the microcrystalline cellulose granules of the comparative examples B and C were dried using a drying process similar to that of Asgharnejad et al., i.e. with heat input, whereas the microcrystalline cellulose granules of Examples 3-5 and 7 were dried using the drying process as claimed in claim 1. Those differences are noted on page 12, lines 32-42 and page 13, line 1 and in Table 2 of the specification.

Table 4, is a comparison of the dissolution of uncompressed time release capsules with the dissolution rate obtained from tablets made using the prior art microcrystalline cellulose drying process (Examples B-C), as well as with tablets made using the microcrystalline cellulose drying process of the present application (Examples 3-5 and 7). To properly gauge the difference between the prior art and the present application each set of data must be compared to the "ideal" dissolution percentages, i.e. the uncompressed controlled-release capsules since the goal of the present invention is to allow time release capsules to be tabletted with a minimum of damage to

the capsules, in order to preserve a release rate that is essentially the same as that of the uncompressed time release capsules.

In the unconditioned batches it can be see that a compression force of 550 kg produces significant damage to the time release capsules of comparative examples B-C, as evidenced by the much faster release of the active ingredient over time. In comparison, a compression force of 560 kg was used to make tablets including the microcrystalline cellulose made by the process of the present invention, and these tablets showed a release rate that is at least 50% closer to the uncompressed controlled-release capsules, than the release rate of the comparative examples B-C. Moreover, in Example 7 the tablets made with the microcrystalline cellulose of the present invention had a release rate that is very close the "ideal" release rate of the uncompressed time release capsules, thereby demonstrating that the microcrystalline cellulose of the present invention was able to cushion the controlled-release particles during tabletting in order to minimize damage thereto.

Table 4 also shows that a significant increase in the compression force (to 700 kg) used to make the tablets using the microcrystalline cellulose of the present invention, yields release rates that are similar to those obtained with tablets compressed with one half the force (350 kg), using the prior art microcrystalline cellulose. This shows that the present invention allows the use of significantly greater compression forces during tabletting than would be feasible using the prior art microcrystalline cellulose.

The conditioned batches show similar improvements in the release rates. Thus, the examples of Table 4 indicate that microcrystalline cellulose of the present invention better preserves the integrity of the controlled-release capsules during granulation, than the microcrystalline cellulose granules made using the drying process of Asgharnejad et al.

In addition to failing to show that Asgharnejad et al. discloses every feature of the process of claim 1 of the present application, the Examiner has also failed to make out a *prima facie* case of obviousness because he has not demonstrated that there is some suggestion or motivation in Asgharnejad et al. for employing a drying step carried out " with no heat input" to remove substantially all of the ethanol from the granules. Finally, the Examiner has also failed to make out a *prima facie* case of obviousness because he has not demonstrated that Asgharnejad et al. provides an expectation of obtaining some benefit, such as improved cushioning granules, by employing a drying step carried out at a controlled rate with no heat input to remove substantially all of the ethanol from the granules. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991), *quoted in* M.P.E.P. § 2143.

Accordingly, for at least the foregoing reasons, the Examiner's rejection of claim 1 over of Asgharnejad et al. should be reversed. Claims 2, 4-8 and 10-13 depend, directly or indirectly, from claim 1. Because claim 1 is not obvious over Asgharnejad et al. for the reasons given above, it follows by statute that claims 2, 4-8 and 10-13 are also not obvious over of Asgharnejad et al. for at least the same reasons. Accordingly, Appellant also respectfully requests that the rejection of claims 2, 4-8 and 10-13 under 35 U.S.C. § 103(a) be reversed.

C. Group II – Claim 3

Claim 3 depends indirectly, from claim 1. Because claim 1 is not obvious over Asgharnejad et al. for the reasons given above, it follows by statute that claim 3 is also not obvious over Asgharnejad et al. for at least the same reasons.

In addition, claim 3 is separately patentable over Asgharnejad et al. because claim 3 requires that the polar organic solvent in the granulating fluid must be isopropanol. Asgharnejad et al. only discloses the use of ethanol. See, col. 3, lines 4-6 of Asgharnejad et al. The Examiner has provided no evidence of any teaching, suggestion or motivation to replace the ethanol of Asgharnejad et al. with isopropanol, as is required by claim 3 of the present application, nor has the Examiner provided any evidence of an expectation of successfully carrying out the process of Asgharnejad et al. using isopropanol in place of ethanol. Accordingly for this additional reason, the rejection of claim 3 should be reversed.

D. Group III – Claim 9

Claim 9 depends indirectly from claim 1. Because claim 1 is not obvious over Asgharnejad et al. for the reasons given above, it follows by statute that claim 9 is also not obvious over Asgharnejad et al. for at least the same reasons.

In addition, claim 9 sets forth the additional limitation that the hydrocolloid is added once substantially all of the polar organic solvent has been removed by the controlled drying step. Asgharnejad et al. does not disclose the addition of a hydrocolloid at this point in the drying step and the Examiner has presented no evidence providing a skilled person with motivation to add a

hydrocolloid at this point in the process, or providing the skilled person with an expectation that some benefit would be obtained by adding a hydrocolloid at this point in the drying step.. Thus, this element of claim 9 is not present in Asgharnejad et al. and claim 9 is separately patentable for this additional reason.

Issue 3: Whether claim 3 is unpatentable under 35 U.S.C. §103(a) over Asgharnejad et al. in view of U.S. Patent No: 6,384,020 issued to Flanner et al. (hereinafter "Flanner et al.").

A. The Rejection

Claim 3 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Asgharnejad et al. as applied claims 1-13, and further in view of Flanner et al. The rationale for this rejection was originally set forth in the Office Action dated July 15, 2003, as follows:

> The information set forth in the Asgharnejad et al patent in the above rejection of the claims under 35 U.S.C. 103 is incorporated into the instant rejection. Instant Claim 3 differs from the Asgharnejad et al patent by claiming isopropanol as the polar organic solvent, which is not disclosed in the Asgharnejad et al patent. However, the Flanner et al patent shows that use of isopropyl alcohol (or isopropanol) as a granulating fluid in processes for the preparation of tablets is well know in the art (see column 5, line 65 of the Flanner et al patent).
>
> Accordingly it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the ethanol used in the granulating fluid in the process of Asgharnejad et al patent with the isopropyl alcohol in view of the recognition in the art, as evidenced by the Flanner et al patent, that use of isopropyl alcohol as a granulating fluid are [sic] effective for preparing free flowing granules that are used in the preparation of tablets.

See page 8, lines 19-29 and page 9 lines 1-2 of the Final Office action dated July 15, 2003.

B. Claim 3 is Patentable over Asgharnejad et al. in View of Flanner et al.

Applicant contends that the 35 U.S.C. § 103(a) rejection based on Asgharnejad et al. in view of Flanner et al. is also overcome for the reasons given above, i.e. at least because Asgharnejad et al. does not disclose the limitation of claim 3 of drying with "no heat input" and Flanner et al. does not cure this deficiency of Asgharnejad et al. since Flanner et al. also lacks a teaching of drying with no heat input. Therefore not all limitations of claim 3 are taught or disclosed in the prior art references and thus the Examiner has not made out a case of *prima facie* obviousness.

In addition, Flanner et al. is directed to rapid immediate release oral dosage forms. See e.g. the title of Flanner et al. The skilled person would thus, not consult Flanner et al. to determine how to make a controlled-release tablet, which is the goal of the present invention, much less incorporate a teaching of Flanner et al. as the Examiner suggests.

Thus for at least these reasons the rejection of claim 3 under 35 U.S.C. §103(a) should be reversed.

Issue 4: Whether Claims 12 and 13 are obvious over Asgharnejad et al. in view of Erkoboni et al.

A. The Rejection

Claims 12 and 13 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Asgharnejad et al. in view of Erkoboni et al. The rationale for this rejection was originally set forth in the Office Action dated July 15, 2003, as follows:

> "The information set forth in the Asgharnejad et al patent in the above rejection of the claims under 35 U.S.C. 103 is incorporated in the instant rejection. Instant claims 12 and 13 differ from Asgharnejad et al patent by disclosing hydrocolloids that are not recited in the Asgharnejad et al patent.
>
> The Erkoboni et al patent shows that the hydrocolloids that are disclosed in the instant claims 12 and 13 are well known in the art. The Erkoboni et al patent discloses microcrystalline cellulose-hydrocolloid compositions and set forth examples of the hydrocolloids in the paragraph bridging column 2 and column 3 of the patent that embraces the listed hydrocolloids in the instant claims 12 and 13. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the starch compound used in the process of the Asgharnejad et al with a hydrocolloid in view of the recognition of the art, as evidenced by Erkoboni et al patent, that the use of hydrocolloids in the preparation of microcrystalline cellulose product are effective for forming an aqueous solution or dispersion."

See page 10, lines 3-16 of the July 15, 2003 Office Action.

B. Group I – Claims 12 and 13

1. The Rejection of Claims 12 and 13 Under 35 U.S.C. §103(a)

Claims 12 and 13 depend from claim 11, which in turn depends from claim 7. Claim 7 depends from claim 1. As discussed above, Applicant submits that claim 1 is patentable over Asgharnejad et al. for at least the reason given above, namely that Asgharnejad et al. does not

teach or suggest the limitation of drying with "no heat input." Applicant contends that the 35 U.S.C. § 103(a) rejection based on Asgharnejad et al. in view of Erkoboni et al. is also overcome for the same reason, i.e. at least because Asgharnejad et al. does not disclose the limitation of claim 3 of drying with "no heat input" and Erkoboni et al. does not cure this deficiency of Asgharnejad et al. Therefore not all limitations of claims 12-13 are taught or disclosed in the prior art references and thus the Examiner has not made out a case of *prima facie* obviousness.

In addition, Erkoboni et al. relates to a microcrystalline cellulose spheronization composition. This is in direct contradiction with claim 1 of the present application which expressly requires that the granulates be made without spheronization. Moreover, spheronization compositions are completely different from the tablets which are the goal of the present invention. In this regard, the hydrocolloid of Erkoboni et al. is used as a spheronizing ingredient for the spheronization compositions. See e.g. col. 3, lines 5-10 of Erkoboni et al. Since the present claims exclude spheronization, the skilled person would not consult Erkoboni et al., much less incorporate a spheronization ingredient of Erkoboni et al. in a cushioning granule that is not to be spheronized, as the Examiner suggests.

Thus for this reason the rejection of claims 12-13 under 35 U.S.C. §103(a) should be reversed.

Issue 5: Whether claims 14-16, and 18-26 are obvious over McTeigue et al.

A. The Rejection

Claims 14-16, and 18-26 have been rejected under 35 U.S.C. §103(a) as being unpatentable over McTeigue et al. More specifically, the Examiner took the position that,

> The McTeigue et al patent discloses microcrystalline cellulose particles having a particle size up to about 220 microns with a particle size standard deviation of from about 75 to about 200 microns (see column 2, line 54), which embraces the microcrystalline cellulose granules of the instant claims.... Although the McTeigue et al patent only discloses the microcrystalline cellulose thereof as having a mean particle size up to 220 microns, the particle size standard deviation of 200 microns that is disclosed in the McTeigue patent does suggests [sic] microcrystalline cellulose particles that have a particle size of at least 250 microns is [sic – are] present in the McTeigue et al patent.... Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant(s) invention to use the microcrystalline cellulose particles of the McTeigue et al patent that have a particle size of 250 microns.

See pages 12-13 of the Final Rejection dated January 15, 2004.

The Examiner has also taken the position that the microcrystalline cellulose described by McTeigue et al., although its mean particle size does not exceed 220 microns, has a "similar utility" and that "[i]t is within the skill of the artisan to screen a desired microcrystalline cellulose particle size [to arrive at the mean particle size range of claim 14 of the present application] in view of their closely related structures and resulting expectation of similar drug coating properties." See the Final Rejection at page 11.

B. The Examiner Has Not Made Out a Case of *Prima Facie* Obviousness

1. Group IV – Claims 14-16, 18 and 20-26

Claim 14 is directed to porous microcrystalline cellulose granules having a loose bulk density of from about 0.2 g/cc to about 0.4 g/cc, and a mean particle size of from about 250 microns to about 1500 microns, made by the process of claim 1.

McTeigue et al. clearly states that the microcrystalline cellulose has an average particle size of about 160 to about 220 microns. See col. 2, line 44 of McTeigue et al. "Mean particle size" and "average particle size" are known to the skilled person as being synonymous. Thus, the range of mean or average particle size disclosed by McTeigue et al. of 160-220 microns, does not overlap with the claimed range of about 250 to about 1500 microns. The Examiner appears to have conceded this point when he stated, "Although the McTeigue et al patent only discloses the microcrystalline cellulose thereof as having a mean particle size of up to about 220 microns..." See page 11, lines 12-14 of the Final Rejection.

However, the Examiner took the position that, "...the particle size standard deviation of 200 microns that is disclosed in the McTeigue patent does suggests [sic] microcrystalline cellulose particles that have a particle size of at least 250 microns is [sic – are] present in the McTeigue et al patent." This statement is simply irrelevant to a determination of the obviousness of claim 14 since claim 14 does not require that the particle size of particular microcrystalline cellulose particles must be at least about 250 microns. Rather, claim 14 requires that the mean particle size of the microcrystalline cellulose must be at least about 250 microns. Thus, although the McTeigue et al. microcrystalline cellulose may contain some individual particles having a

particle size in excess of 250 microns, this does not render claim 14 obvious because McTeigue et al. clearly discloses that the average or mean particle size of its microcrystalline cellulose should be from 160-220 microns, which is significantly outside the range claimed in claim 14 of the present application of about 250 to about 1500 microns.

The Examiner also took the position that,

> Furthermore, regarding the differences in particle size [sic – mean particle size] of the microcrystalline cellulose, there is a distinction between a new article of commerce and a new article, which is patentable. Any change in form may render an article new in commerce. But to be patentable it must be more efficacious or possess new properties by a combination with other ingredients and not merely change form, which has the advantages which one skilled in the art would expect from the change. (Citation omitted). Accordingly, it would have been obvious to one of ordinary skill in the art t the time of Applicant(s) [sic] invention to use the microcrystalline cellulose particles of the McTeigue et al patent that have a particle size of 250 microns, in view of their closely related structures and the resulting expectation of similar drug coatings.

See Final Office Action dated January 15, 2004 page 11.

First, McTeigue et al. does not set forth a similar utility for the microcrystalline cellulose as in the present application, i.e. for cushioning controlled release particles during the tabletting process to help preserve their controlled release characteristics. In fact, a close reading of McTeigue et al. demonstrates that the microcrystalline cellulose of McTeigue et al. is used for a totally different purpose than the microcrystalline cellulose of the present invention.

More specifically, McTeigue et al. clearly teaches that,

> The present invention is directed to a particle which comprises a seed core comprised primarily of microcrystalline cellulose, ... to which a pharmaceutically active ingredient in solution is layered onto the microcrystalline cellulose by spray coating.

See col. 1, lines 40-45 of McTeigue et al. Thus, in the McTeigue et al. pharmaceutical composition, the microcrystalline cellulose forms a seed core and the pharmaceutically active ingredient is spray coated onto the microcrystalline cellulose. In contrast, the utility of the granules of the present invention is as a cushioning agent for controlled-release particles in pharmaceutical compositions wherein the pharmaceutically active ingredient is included in controlled release particles and the controlled release particles and microcrystalline cellulose granules are formed into a tablet by tabletting them together under high pressure. See e.g. page 3, line 21 to page 4, line 9 of the specification. As a result, there is no disclosure in McTeigue et al. that the microcrystalline cellulose of McTeigue et al. needs to have certain properties sufficient to provide cushioning of controlled release particles during a tabletting operation.

Secondly, the Examiner says that, "It is within the skill of the artisan to screen a desired microcrystalline cellulose particle size [of McTeigue et al.] [in order to arrive at the mean particle size of claim 14 of the present application]." See the Final Office action page 11. There is a major flaw in the Examiner's reasoning. Specifically, if a skilled person were to select a mean particle size of the microcrystalline cellulose granules based on the teachings of McTeigue et al. for optimum effectiveness, the skilled person would follow the express teachings of McTeigue et al. that the preferred source of microcrystalline cellulose has an average or mean particle size of 180 microns, and therefore would use an average or mean particle size of about 180 microns when optimizing the McTeigue et al. composition. See e.g. col. 2, lines 40-41 and 48-50 of McTeigue et al. As a result, optimization of the mean or average particle size of the

McTeigue et al. microcrystalline cellulose leads a skilled person further away from the claimed invention, rather than to the claimed invention, as the Examiner suggests.

Therefore, the Examiner has not set forth a *prima facie* case of obviousness against claim 14 of the present application.

Claims 15-16, 18 and 20-26 depend, directly or indirectly, from claim 14. Because claim 14 is not obvious over McTeigue et al. for the reasons given above, it follows by statute that claims 15-16, 18 and 20-26 are also not obvious over McTeigue et al. for at least the same reasons. Accordingly, Appellant respectfully requests that the rejection of claims 14-16, 18 and 20-26 under 35 U.S.C. § 103(a) be reversed.

2. Group V – Claim 19

Claim 19 depends indirectly, from claim 14. Because claim 14 is not obvious over McTeigue et al. for the reasons given above, it follows by statute that claim 19 is also not obvious over McTeigue et al. for at least the same reasons.

In addition, claim 19 is separately patentable over McTeigue et al. since the mean particle size range of claim 19 is from about 400 microns to about 900 microns. There is no teaching, suggestion or motivation anywhere in McTeigue et al. to employ a mean particle size in this range or anywhere close to this range, since the upper limit of the mean or average particle size disclosed in McTeigue et al. is 220 microns, as discussed above. Moreover, the Examiner has completely failed to set out any case of obviousness against the subject matter of claim 19, much less a case of *prima facie* obviousness, since the Examiner has nowhere even alleged, much less

supported with evidence, that it would be obvious to modify the teachings of McTeigue et al. to arrive at microcrystalline cellulose having a mean or average particle size of at least about 400 microns.

Accordingly, for the foregoing reasons, the rejection of claim 19 under 35 U.S.C. §103(a) over McTeigue et al. should be reversed.

Issue 6: Whether Claim 17 is obvious over McTeigue et al. in view of Kumar.

A. The Rejection

Claim 17 has been rejected under 35 U.S.C. §103(a) as being unpatentable over McTeigue et al. in view of Kumar. More specifically, in support of the rejection of claim 17, the Examiner relies on the disclosure of McTeigue et al., as discussed above with respect to Issue 5. See page 12, lines 1-2 of the Final Rejection. The Kumar patent is cited by the Examiner to support the proposition that microcrystalline cellulose with a density range of 0.20 to 0.45 g/ml is well known in the art, based on col. 5, lines 46-48 of Kumar. See the Final Rejection at page 12, lines 10-13. From this, the Examiner concludes that,

> ...it would have been obvious to one having ordinary skill in the art to substitute the microcrystalline cellulose having a density of 0.4 g/cc of the McTeigue et al patent for the microcrystalline cellulose that comprises a density range of 0.20 to 0.45 g/ml of the Kumar patent, in view of the recognition in the art, as evidenced by the Kumar patent, that microcrystalline cellulose has inherent binding and superior tableting flow properties.

See page 12 of the Final Rejection.

B. Group VI – Claim 17

Claim 17 depends directly from claim 16. As discussed above, claim 16 is directed to porous microcrystalline cellulose granules having an irregular shape, a loose bulk density of from about 0.2 g/cc to about 0.4 g/cc, and a mean particle size of from about 250 microns to about 1500 microns.

As noted above, McTeigue et al. neither teaches nor suggests microcrystalline cellulose having a mean particle size greater than 220 microns. See col. 1, lines 54-55 of McTeigue et al.. Kumar teaches that the microcrystalline cellulose should have a density of 0.2 g/ml to 0.45 g/ml and a particle size range of 150-200 microns. See col. 9, lines 21-22 of Kumar. Thus, the mean or average particle size of the microcrystalline cellulose of Kumar must be within the range of 150-200 microns since it is mathematically impossible for the average or mean particle size to fall outside of the overall particle size range due to the methodology used to calculate mean or average particle size, i.e. summing the sizes of all of the particles in the composition and dividing by the total number of particles in the composition. Accordingly, viewed in a light most favorable to the Examiner's position, Kumar discloses microcrystalline cellulose having an average or mean particle size of 150-200 microns.[2]

The Examiner concludes that it would be obvious to substitute the microcrystalline cellulose of McTeigue et al. for the microcrystalline cellulose of Kumar in order to arrive at the present invention. This argument fails since neither Kumar nor McTeigue et al. teaches or

[2] Note that for the microcrystalline cellulose of Kumar to have an average or mean particle size of 200 microns, all of the particles would have to be of the identical size of 200 microns, to meet the criteria of Kumar that the microcrystalline cellulose must have a particle size in the range of 150-200 microns.

suggests the microcrystalline cellulose of the present invention, i.e. having a mean particle size of at least about 250 microns. Thus, in the applicant's view, it matters not whether the microcrystalline cellulose of McTeigue et al. or the microcrystalline cellulose of Kumar is employed, the skilled person simply cannot arrive at the present invention since neither Kumar nor McTeigue et al. disclose microcrystalline cellulose having a mean particle size of at least about 250 microns.

As stated above, a *prima facie* case of obviousness has not been made out when the prior art does not teach or suggest every limitation of the pending claim. By statute, claim 17 includes every limitation of claim 16. Thus, McTeigue et al. and Kumar do not teach or suggest every limitation of claim 17 since the mean particle size limitation of claim 17 is not taught by either of these references as discussed above. Moreover, there is no teaching, suggestion or motivation in either McTeigue et al. or Kumar to adjust the mean particle size of the microcrystalline cellulose granules in order to arrive at the mean particle size range of the claimed invention. Rather, following the preferred embodiment of McTeigue et al., for example, the skilled person would be led to a mean particle size of 180 microns, which is further away from the mean particle size claimed in claim 17. Finally, there is no teaching or suggestion in either McTeigue et al. or Kumar which would lead a skilled person to expect a beneficial result from increasing the mean particle size of the microcrystalline cellulose granules to at least about 250 microns.

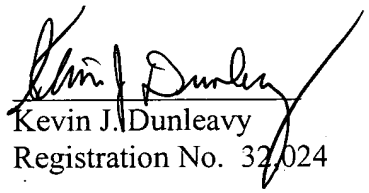
Therefore, it follows that the Examiner has not set forth a *prima facie* case of obviousness since none of the three elements of a *prima facie* case is found in the references relied on by the

Examiner. Accordingly, Appellant respectfully requests that the rejection of claim 17 as obvious over McTeigue et al. and Kumar be reversed for at least these reasons.

IX. Conclusion

For the foregoing reasons, Appellant respectfully submits that each of the rejections should be reversed, and that the pending claims should be allowed. Such a decision is respectfully solicited.

Respectfully submitted,



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APPENDIX: THE CLAIMS ON APPEAL

1. A method for preparing porous microcrystalline cellulose granules comprising the following steps:

(a) granulating microcrystalline cellulose with a granulating fluid comprising water and a water-miscible, volatile, polar organic solvent to provide a granulated microcrystalline cellulose;

(b) drying the granulated microcrystalline cellulose at a controlled rate with no heat input at ambient temperature for a time sufficient to remove at least substantially all of the polar organic solvent from the granulated microcrystalline cellulose without removing at least a substantial portion of the water from the granulated microcrystalline cellulose, and without extruding or spheronizing the granulated microcrystalline cellulose from granulation step (a); and

(c) subsequent to step (b), removing at least a substantial portion of the water from the granulated microcrystalline cellulose.

2. The method of claim 1 wherein said polar organic solvent is selected from the group consisting of methanol, ethanol, propanol, isopropanol, t-butyl alcohol and acetone.

3. The method of claim 2 wherein said polar organic solvent is isopropanol.

4. The method of claim 1 wherein the volume ratio of water to said polar organic solvent in said granulating fluid is from 85:15 to 15:85.

5. The method of claim 1 wherein the ratio of said granulating fluid to said microcrystalline cellulose in the granulating step is from 1:2 to 2:1.

6. The method of claim 1 wherein said granulated microcrystalline cellulose is initially dried at controlled temperature and pressure and once substantially all of the polar organic solvent is removed, further drying is carried out at one or more of an elevated temperature, reduced pressure or both.

7. The method of claim 1 further comprising the step of adding to the granulated microcrystalline cellulose about 1 to about 30% by weight of a hydrocolloid, based on the weight of the granulated microcrystalline cellulose.

8. The method of claim 7 wherein the hydrocolloid is added to the granulated microcrystalline cellulose prior to the drying step which removes substantially all of the polar organic solvent component from the granulated microcrystalline cellulose.

9. The method of claim 7 wherein the hydrocolloid is added to the microcrystalline cellulose granules after substantially all of the polar organic solvent has been removed from the granulated microcrystalline cellulose.

10. The method of claim 7 wherein in the adding step the hydrocolloid is coated onto the surface of the microcrystalline cellulose granules.

11. The method of claim 7 wherein the hydrocolloid comprises one or more hydrocolloids selected from the group consisting of: methylcellulose, hydroxypropyl cellulose, sodium carboxymethylcellulose, hydroxypropyl methylcellulose, gelatin, water soluble cellulose acetate, polyvinyl pyrrolidone, starches, alginates, alginic acid, locust bean seed extract, guar seed extract, carrageenan, gum tragacanth, gum arabic and gum karoya.

12. The method of claim 11 wherein the hydrocolloid is selected from the group consisting of polyvinyl pyrrolidone, methylcellulose, hydroxypropyl cellulose and hydroxypropyl methylcellulose.

13. The method of claim 11 wherein the hydrocolloid comprises polyvinyl pyrrolidone.

14. Porous, granulated microcrystalline cellulose made by the process of claim 1 having a loose bulk density of from about 0.2 g/cc to about 0.4 g/cc, and a mean particle size of from about 250 microns to about 1500 microns.

15. Porous, granulated microcrystalline cellulose made by the process of claim 7 having a loose bulk density of from about 0.2 g/cc to about 0.4 g/cc, and a mean particle size of from about 250 microns to about 1500 microns.

16. Porous microcrystalline cellulose granules having an irregular shape, a loose bulk density of from about 0.2 g/cc to about 0.4 g/cc, and a mean particle size of from about 250 microns to about 1500 microns.

17. Microcrystalline cellulose granules as claimed in claim 16 having a loose bulk density of from about 0.25 to about 0.35 g/cc.

18. Microcrystalline cellulose granules as claimed in claim 16 having a mean particle size of from about 250 microns to about 1000 microns.

19. Microcrystalline cellulose granules as claimed in claim 16 having a mean particle size of from about 400 microns to about 900 microns.

20. Microcrystalline cellulose granules as claimed in claim 16 further comprising from about 1% to about 30% by weight, of a hydrocolloid, based on the weight of the granulated microcrystalline cellulose.

21. Microcrystalline cellulose granules as claimed in claim 20 wherein the hydrocolloid comprises one or more hydrocolloids selected from the group consisting of: methylcellulose, hydroxypropyl cellulose, sodium carboxymethylcellulose, hydroxypropyl methylcellulose, gelatin, water soluble cellulose acetate, polyvinyl pyrrolidone, starches, alginates, alginic acid, locust bean seed extract, guar seed extract, carrageenan, gum tragacanth, gum arabic and gum karoya.

22. Microcrystalline cellulose granules as claimed in claim 21 wherein the hydrocolloid is selected from the group consisting of polyvinyl pyrrolidone, methylcellulose, hydroxypropyl cellulose and hydroxypropyl methylcellulose.

23. Microcrystalline cellulose granules as claimed in claim 21 wherein the hydrocolloid comprises polyvinyl pyrrolidone.

24. A tablet which comprises from about 5% to about 80% by weight of granulated microcrystalline cellulose as claimed in claim 16; from about 5% to about 80% by weight of one or more of controlled release particles and barrier coated materials which contain an active ingredient; and from 0% to about 20% by weight of other excipients, based on the total weight of the tablet.

25. A tablet which comprises from about 5% to about 80% by weight of granulated microcrystalline cellulose as claimed in claim 20; from about 5% to about 80% by weight of one or more of controlled release particles and barrier coated materials which contain

an active ingredient; and 0% to about 20% by weight of other excipients, based on the total weight of the tablet.

26. A tablet which comprises from about 5% to about 80% by weight of granulated microcrystalline cellulose as claimed in claim 23; from about 5% to about 80% by weight of one or more of controlled release particles and barrier coated materials which contain an active ingredient; and 0% to about 20% by weight of other excipients, based on the total weight of the tablet.